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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,280	09/09/2003	William M. Canfield	241990US77DIV	1393

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EXAMINER	
SAIDHA, TEKCHAND	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,280	CANFIELD, WILLIAM M.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 2003* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Preliminary Amendment filed 9.9.2003 has been entered. Accordingly claims 1-39 have been cancelled. New claims 40-68 have been added. Claims 40-68 are pending and under consideration in this examination.

2. ***Priority***

Acknowledgment is made of applicants' filling of a divisional based on US Serial No. 09/636,060 [filed 08/10/2000, now US Patent 6,642,038], which claims the benefit of 60/153,831, filed 09/14/1999.

3. Claims 63-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) 63-68 contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 63-68 are directed to N-acetylglucosamine-1-phosphotransferase having varying specific activities and compositions comprising N-acetylglucosamine-1-phosphotransferase having such activities. The original specification does not contain any description of the various specific activities, for example, 10^6 pmol/h/mg, or $5X10^6$ pmol/h/mg and so on. The specification discloses no such activities, and one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. This is a new matter situation, wherein the new matter has been added only to the claims, hence this rejection.

4. ***Enablement Rejection***

Claims 40, 44, 48, 50, 52, 56, 58, 60, 62-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated N-acetylglucosamine-1-phosphotransferase comprising αβγ-subunits disclosed in the sequences of SEQ ID NO : 1, 2 & 3 respectively, does not reasonably provide enablement for : any N-acetylglucosamine-1-phosphotransferase from any source [claims 63-68); or a subunit of N-acetylglucosamine-1-phosphotransferase having 70% homology to SEQ ID NO : 1 or SEQ ID NO: 2 or SEQ ID NO: 3 [40, 44, 48, 50, 52, 56, 58, 60, 62].

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988))[*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are [the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

The specification provides guidance and examples for making an α- or -β or γ-subunits of N-acetylglucosamine-1-phosphotransferase comprising SEQ ID NO: 1, 2 or 3. However, the specification does not teach specific molecules of these sequences or does not teach the specific structural/catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered. The state of the art as exemplified by Attwood et al. [Comput. Chem. 2001, col. 54(4), pp. 329-39] is such that "..we do not fully understand the

rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given the knowledge only of its sequence or structure in isolation" (see abstract and the entire publication). Further Ponting [Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29] states that "...predicting function by homology is a qualitative, rather than quantitative process and requires particular care to be taken, due attention should be paid to all available clues to function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domain in proteins" (see abstract and the entire publication).

The standard of meeting enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed polynucleotide is enormous and entails selecting specific nucleotides to change (deletion, insertion, substitution or combination thereof) in a polynucleotide to make a claimed polynucleotide and determining by assays whether the polypeptide has activity. The specification does not provide guidance with respect to the specific structural/catalytic amino acids and the structural motifs essential for enzyme structure/function which must be preserved. Thus, searching for the specific nucleotides to change (deletion, insertion, substitution or combination thereof) in a polynucleotide to encode polypeptide that is at least 70% identical to each of the sununits [α- or -β or γ-subunits of N-acetylglucosamine-1-phosphotransferase] or the enzyme as a whole, is well outside the realm of routine experimentation and predictability in the art of success in determining whether the resulting polypeptide has activity is extremely low since no guidance is provided with respect to the structural motifs essential for enzyme structure and activity/function which must be preserved. Further, the meaning of the phrase 'biologically active', is a protein having different activities, including, enzymatic or immunological. These α- or -β or γ-subunits of N-acetylglucosamine-1-phosphotransferase have been shown to possess only the

activity of N-acetylglucosamine-1-phosphotransferase. No separate biological activity has been shown to be associated with each of the subunits (see claim 48, 52, 56, 60).

Determining the biological function(s) would be highly unpredictable as no specific α- or -β or γ-subunits of N-acetylglucosamine-1-phosphotransferase function or enzyme assay using a particular substrate has been shown to be associated with the subunits of SEQ ID NO: 1-3.

Therefore, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific catalytic amino acids and structural motifs essential for activity/function which must be preserved in order to alter or modify the sequences by 30% as claimed; or obtain the various α- or -β or γ-subunits of N-acetylglucosamine-1-phosphotransferase from any source, or obtain the recited specific activities, with no guidance to any purification scheme(s). Without such a guidance, the experimentation left to those skilled in the art is undue.

5. **Written Description**

Claims 63-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of N-acetylglucosamine-1-phosphotransferase from any source, with no defined structure associated with it.

The specification describes α- or -β or γ-subunits of <u>human</u> N-acetylglucosamine-1-phosphotransferase in SEQ ID NO: 1-3, or a single enzyme species having 3 subunits. The specification does not contain any disclosure or description of the structure and function from a representative number of species in order to comprise a genus. N-acetylglucosamine-1-phosphotransferase is a class of enzyme that will utilize distinct substrate(s),

such as UDP-GlcNAc-, or acceptor molecule such as, alpha-methylmannoside [see, for example, JBC, 271(49):31446-31451, 1996]. The same enzyme from different source have distinct substrate specificities. Further the specific activities, as claimed, vary depending upon the substrate used. Therefore, without clear description of the substrate(s) involved, the basis for description of the specific activities remains undefined & un-possessed. The species of polypeptides subunits that make N-acetylglucosamine-1-phosphotransferase molecule is a small species group, rather than a genus, and is therefore insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus, and to be representative of N-acetylglucosamine-1-phosphotransferase from any source, wherein, no predictability of the structure is apparent. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

6. Applicant is advised that should claim 54 be found allowable, claim 54 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

7. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 63-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Bao et al. [JBC, 271(49):31446-31451, 1996]. Bao et al. teach isolation to homogeneity a bovine N-acetylglucosamine-1-phosphotransferase. Applicants' claims are drawn N-acetylglucosamine-1-phosphotransferase from any source having a certain specific activity. Since the specific activity can vary depending upon the source, substrate specificity [see figure 3, using 2 different substrates], reaction conditions, such as temperature, pH or buffer, it is impossible to obtain a defined specific activity as claimed from any source. Also it is known that specific activity is a measure of purity. The higher the purity of the enzyme, higher the specific activity, assuming the enzyme is stable. Therefore, the homogeneous preparation of Bao et al. will inherently have a very high specific activity, and baring teachings to the contrary, will meet the specific activity claim limitations. Further, Bao et al. teach the presence of the purified bovine N-acetylglucosamine-1-phosphotransferase in a cocktail solution containing a buffer and a variety of carriers will meet the composition claim limitations, since the exact nature of the composition or carrier remains undefined. It is not possible for the Examiner to physically compare the claimed N-acetylglucosamine-1-phosphotransferase and the N-acetylglucosamine-1-phosphotransferase of Boa et al., since the PTO has no such facilities. Applicant bears the burden of providing evidence which distinguishes the claimed enzyme from that disclosed by Bao et al. A preferred means of providing this evidence is for applicant to submit a side-by-side comparison between the enzyme of the prior art and the claimed enzyme which demonstrates any material differences and shows the claimed N-acetylglucosamine-1-phosphotransferase to be distinct in view of the N-acetylglucosamine-1-phosphotransferase of the prior art.

8. ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so

as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 40-68 are rejected under the judicially created doctrine of double patenting over claims 13-25 & 34-42 of U. S. Patent No. 6,670,165 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The instant claims are drawn to a broader scope (genus) of the already allowed narrower claims (species). The genus claims are anticipated by the species claims for the following reasons : The claimed product claims comprises N-acetylglucosamine-1-phosphotransferase which are 70% identical to SEQ ID Nos. 1-3. These claimed sequences are 100% identical to the patented product claims comprising modified lysosomal hydrolase (a broader term) of SEQ ID Nos. 1-3.

9. Claims 40-68 are rejected under the judicially created doctrine of double patenting over claims 9-13, 19 & 24 of U. S. Patent No. 6,534,100 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The instant claims are drawn to a broader scope (genus) of the already allowed narrower claims (species). The genus claims are anticipated by the species claims for the following reasons : The claimed product claims comprises N-acetylglucosamine-1-phosphotransferase which are 70% identical to SEQ ID Nos. 1-3. These claimed sequences are 100% identical to the patented product claims comprising lysosomal hydrolase (a broader term) of SEQ ID Nos. 1-3.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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